

## IN THE CLAIMS:

Please amend claims 1, 6, 7, 21, 46, 307, 348 and 356, cancel claims 5 and 279 without prejudice or disclaimer, and add claims 357-361. This listing of claims replaces all prior listings of claims.

## LISTING OF CLAIMS:

1. (Currently Amended) An isolated interferon (IFN) alpha cytokine, comprising an amino acid replacement in its sequence of amino acids, ~~whereby the interferon-alpha cytokine exhibits increased resistance to proteolysis compared to the unmodified interferon alpha cytokine that does not comprise the amino acid replacement~~, wherein:

an amino acid replacement is E41Q, whereby the interferon alpha cytokine exhibits increased resistance to proteolysis compared to the unmodified interferon alpha cytokine that does not comprise the amino acid replacement; and or the corresponding position, based upon alignment, in the interferon-alpha cytokine;

the interferon is not glycosylated at E41Q; and

the unmodified interferon alpha cytokine is selected from among an interferon  $\alpha$ -2b (IFN $\alpha$ -2b), an interferon  $\alpha$ -2a (IFN $\alpha$ -2a), an interferon  $\alpha$ -2c (IFN $\alpha$ -2c) and consensus interferon whose sequences are set forth in SEQ ID Nos. 1, 182, 185 and 232, respectively.

2-5. (Cancelled)

6. (Currently Amended) ~~An interferon alpha cytokine of claim 1, wherein:~~  
~~the modification is E41Q and is selected from among IFN $\alpha$ -2b, IFN $\alpha$ -2a, IFN $\alpha$ -2c, consensus interferon, IFN $\alpha$ -c, IFN $\alpha$ -d, IFN $\alpha$ -5, IFN $\alpha$ -6, IFN $\alpha$ -4, IFN $\alpha$ -4b, IFN $\alpha$ -I, IFN $\alpha$ -J, IFN $\alpha$ -H, IFN $\alpha$ -F and IFN $\alpha$ -8, each comprising the modification E41Q;~~ wherein:

~~the sequence of a human wild-type interferon alpha for each of IFN $\alpha$ -2b, IFN $\alpha$ -2a, IFN $\alpha$ -2c, consensus interferon, IFN $\alpha$ -c, IFN $\alpha$ -d, IFN $\alpha$ -5, IFN $\alpha$ -6, IFN $\alpha$ -4, IFN $\alpha$ -4b, IFN $\alpha$ -I, IFN $\alpha$ -J, IFN $\alpha$ -H, IFN $\alpha$ -F and IFN $\alpha$ -8; is set forth in SEQ ID Nos. 1, 182, 185, 232, 183 and 186-195, respectively;~~

the interferon alpha cytokine is not glycosylated at E41Q; and

residue 1 in each SEQ ID corresponds to residue 1 of the mature interferon-alpha .

7. (Currently Amended) The interferon alpha cytokine of claim ~~6~~, wherein:  
the unmodified interferon alpha cytokine is selected from among an interferon  $\alpha$ -2b (IFN $\alpha$ -2b), an interferon  $\alpha$ -2a (IFN $\alpha$ -2a) , an interferon  $\alpha$ -2c (IFN $\alpha$ -2c) and a consensus interferon alpha .

8. (Previously Presented) An interferon alpha cytokine of claim 6, further comprising duo-amino acid replacements selected from among:

D by N at position 2 and P by S at position 4;  
D by N at position 2 and P by T at position 4;  
L by N at position 3 and Q by S at position 5;  
L by N at position 3 and Q by T at position 5;  
P by N at position 4 and T by S at position 6;  
P by N at position 4 and T by T at position 6;  
Q by N at position 5 and H by S at position 7;  
Q by N at position 5 and H by T at position 7;  
T by N at position 6 and S by S at position 8;  
T by N at position 6 and S by T at position 8;  
H by N at position 7 and L by S at position 9;  
H by N at position 7 and L by T at position 9;  
S by N at position 8 and G by S at position 10;  
S by N at position 8 and G by T at position 10;  
L by N at position 9 and S by S at position 11;  
L by N at position 9 and S by T at position 11;  
M by N at position 21 and K by S at position 23;  
M by N at position 21 and K by T at position 23;  
R by N at position 22 and I by S at position 24;  
R by N at position 22 and I by T at position 24;  
R or K by N at position 23 and S by S at position 25;  
R or K by N at position 23 and S by T at position 25;  
I by N at position 24 and L by S at position 26;  
I by N at position 24 and L by T at position 26;  
S by N at position 25 and F by S at position 27;  
S by N at position 25 and F by T at position 27;  
L by N at position 26 and S by S at position 28;  
L by N at position 26 and S by T at position 28;  
S by N at position 28 and L by S at position 30;  
S by N at position 28 and L by T at position 30;  
L by N at position 30 and D by S at position 32;

L by N at position 30 and D by T at position 32;  
K by N at position 31 and R by S at position 33;  
K by N at position 31 and R by T at position 33;  
D by N at position 32 and H by S at position 34;  
D by N at position 32 and H by T at position 34;  
R by N at position 33 and D by S at position 35;  
R by N at position 33 and D by T at position 35;  
H by N at position 34 and F by S at position 36;  
H by N at position 34 and F by T at position 36;  
D by N at position 35 and G by S at position 37;  
D by N at position 35 and G by T at position 37;  
F by N at position 36 and F by S at position 38;  
F by N at position 36 and F by T at position 38;  
G by N at position 37 and P by S at position 39;  
G by N at position 37 and P by T at position 39;  
F by N at position 38 and Q by S at position 40;  
F by N at position 38 and Q by T at position 40;  
P by N at position 39 and E by S at position 41;  
P by N at position 39 and E by T at position 41;  
Q by N at position 40 and E by S at position 42;  
Q by N at position 40 and E by T at position 42;  
E by N at position 41 and F by S at position 43;  
E by N at position 41 and F by T at position 43;  
E by N at position 42 and G by S at position 44;  
E by N at position 42 and G by T at position 44;  
F by N at position 43 and N by S at position 45;  
F by N at position 43 and N by T at position 45;  
G by N at position 44 and Q by S at position 46;  
G by N at position 44 and Q by T at position 46;  
N by N at position 45 and F by S at position 47;  
N by N at position 45 and F by T at position 47;  
Q by N at position 46 and Q by S at position 48;  
Q by N at position 46 and Q by T at position 48;

F by N at position 47 and K by S at position 49;  
F by N at position 47 and K by T at position 49;  
Q by N at position 48 and A by S at position 50;  
Q by N at position 48 and A by T at position 50;  
K by N at position 49 and E by S at position 51;  
K by N at position 49 and E by T at position 51;  
A by N at position 50 and T by S at position 52;  
A by N at position 50 and T by T at position 52;  
S by N at position 68 and K by S at position 70;  
S by N at position 68 and K by T at position 70;  
K by N at position 70 and S by S at position 72;  
K by N at position 70 and S by T at position 72;  
A by N at position 75 and D by S at position 77;  
A by N at position 75 and D by T at position 77;  
D by N at position 77 and T by S at position 79;  
D by N at position 77 and T by T at position 79;  
I by N at position 100 and G by S at position 102;  
I by N at position 100 and G by T at position 102;  
Q by N at position 101 and V by S at position 103;  
Q by N at position 101 and V by T at position 103;  
G by N at position 102 and G by S at position 104;  
G by N at position 102 and G by T at position 104;  
V by N at position 103 and V by S at position 105;  
V by N at position 103 and V by T at position 105;  
G by N at position 104 and T by S at position 106;  
G by N at position 104 and T by T at position 106;  
V by N at position 105 and E by S at position 107;  
V by N at position 105 and E by T at position 107;  
T by N at position 106 and T by S at position 108;  
T by N at position 106 and T by T at position 108;  
E by N at position 107 and P by S at position 109;  
E by N at position 107 and P by T at position 109;  
T by N at position 108 and I by S at position 110;

T by N at position 108 and I by T at position 110;  
K by N at position 134 and S by S at position 136;  
K by N at position 134 and S by T at position 136;  
S by N at position 154 and N by S at position 156;  
S by N at position 154 and N by T at position 156;  
T by N at position 155 and L by S at position 157;  
T by N at position 155 and L by T at position 157;  
N by N at position 156 and Q by S at position 158;  
N by N at position 156 and Q by T at position 158;  
L by N at position 157 and E by S at position 159;  
L by N at position 157 and E by T at position 159;  
Q by N at position 158 and S by S at position 160;  
Q by N at position 158 and S by T at position 160;  
E by N at position 159 and L by S at position 161;  
E by N at position 159 and L by T at position 161;  
S by N at position 160 and R by S at position 162;  
S by N at position 160 and R by T at position 162;  
L by N at position 161 and S by S at position 163;  
L by N at position 161 and S by T at position 163;  
R by N at position 162 and K by S at position 164;  
R by N at position 162 and K by T at position 164;  
S by N at position 163 and E by S at position 165; and  
S by N at position 163 and E by T at position 165.

9.-20. (Cancelled)

21. (Currently Amended) An interferon alpha cytokine of claim 6 ~~4~~, comprising two, three, four or five amino acid replacements in its sequence of amino acids.

22. (Previously presented) The interferon alpha cytokine of claim 21 that is a modified IFN $\alpha$ -2b cytokine.

23-39. (Cancelled)

40. (Original) A pharmaceutical composition, comprising a cytokine of claim 1 in a pharmaceutically acceptable carrier.

41-45. (Cancelled)

46. (Withdrawn, Currently Amended) An interferon alpha cytokine of claim 61, selected from among an IFN $\alpha$ -2a, an IFN $\alpha$ -c, an IFN $\alpha$ -2c, an IFN $\alpha$ -d, an IFN $\alpha$ -5, an IFN $\alpha$ -6, an IFN $\alpha$ -4, an IFN $\alpha$ -4b, an IFN $\alpha$ -I, an IFN $\alpha$ -J, an IFN $\alpha$ -H, an IFN $\alpha$ -F, an IFN $\alpha$ -8, and an IFN $\alpha$ -consensus cytokine.

47.- 306. (Cancelled)

307. (Currently Amended) An interferon alpha cytokine of claim 1 that is an IFN $\alpha$ -2b: ~~E by Q at position 41.~~

308. -340. (Cancelled)

341. (Previously Presented) The interferon alpha cytokine of claim 1 that contains only a single amino acid replacement compared to the interferon cytokine that does not include the E41Q replacement.

342. (Cancelled)

343. (Previously Presented) The pharmaceutical composition of claim 40, formulated for oral administration.

344. (Cancelled)

345. (Previously Presented) An interferon alpha cytokine, comprising the sequence of amino acids set forth in SEQ ID NO:87.

346. (Cancelled)

347. (Previously Presented) The interferon alpha cytokine of claim 1, comprising two amino acid replacements.

348. (Currently Amended) A modified interferon (IFN) alpha cytokine of claim 6, comprising one or two amino acid replacements, ~~wherein one replacement is E41Q.~~

349. (Previously Presented) The modified IFN alpha cytokine of claim 348 that is an IFN- $\alpha$ 2b cytokine.

350. (Previously Presented) A pharmaceutical composition, comprising a cytokine of claim 348 in a pharmaceutically acceptable carrier.

351. (Previously Presented) A pharmaceutical composition, comprising a cytokine of claim 349 in a pharmaceutically acceptable carrier.

352. (Previously Presented) A pharmaceutical composition, comprising a cytokine of claim 307 in a pharmaceutically acceptable carrier.

353. (Previously Presented) The pharmaceutical composition of claim 352 that is formulated as a tablet or capsule for oral administration.

354. (Previously Presented) A pharmaceutical composition, comprising a cytokine of claim 345 in a pharmaceutically acceptable carrier.

355. (Previously Presented) The modified interferon alpha cytokine of claim 22, comprising amino acid replacements corresponding to E41Q and D94G.

356. (Currently Amended) A pharmaceutical composition, comprising a The modified interferon alpha cytokine of claim 6, ~~wherein the unmodified interferon alpha cytokine is selected from among an interferon  $\alpha$  2b (IFN $\alpha$  2b), an interferon  $\alpha$  2a (IFN $\alpha$  2a), an interferon  $\alpha$  2c (IFN $\alpha$  2c) and consensus interferon.~~

357. (New) The pharmaceutical composition of claim 354 that is formulated for oral administration.

358. (New) The pharmaceutical composition of claim 357 that is formulated as tablet or capsule.

359. (New) The interferon alpha cytokine of claim 6 that contains only a single amino acid replacement compared to the interferon cytokine that does not include the E41Q replacement.

360. (New) The pharmaceutical composition of claim 356 that is formulated for oral administration.

361. (New) The pharmaceutical composition of claim 360 that is formulated as a tablet or capsule.